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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/060,188	04/14/1998	DOMINIC P. BEHAN		9333

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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/060,188	BEHAN ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,40 and 45-74* is/are pending in the application.

4a) Of the above claim(s) *71-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,40 and 45-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *34,40 and 45-74* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10/18/05 has been entered in full. Claims 34, 40, 45, 52, 53, 60, 63-66, 69 and 70 are amended. Claims 1-33, 35-39 and 41-44 were previously canceled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims 71-74 drawn to an invention nonelected without traverse in Applicant's response filed 10/14/1999. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 34, 40, and 45-70 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (4/19/2005).

The rejection of claims 34, 40 and 45-70 under 35 U.S.C § 112, second paragraph, at pg 11-12 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to claims 63-66, 69 and 70.

The rejection of claims 34, 45, 49-51, 61 and 69 under 35 U.S.C. § 103 at pg 16-18 as being unpatentable over Teitler (US Patent 6,255,089) in view of O'Dowd (1995) is *withdrawn* upon further consideration by the examiner.

The rejection of claims 52, 62, 67 and 69 under 35 U.S.C. § 103 at pg 16-18 as being unpatentable over Teitler (US Patent 6,255,089) in view of Scheer 1997) and in further view of Xu (1996) is *withdrawn* upon further consideration by the examiner.

Claim Rejections - 35 USC § 101, utility

Claims 34, 40 and 45-70 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Applicants' arguments (10/18/05; pg 7-11) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 10/18/05, Applicants argue that the Office Action has not established a prima facie showing that there is no substantial or "real world" utility. Applicants argue that the Office Action states there is no substantial utility but "without any support for factual findings and without evaluating all the relevant evidence of record" (pg 8). Applicants submit that relevant evidence of record, specifically the Watson Declaration filed 11/2/2000 (Exhibit 1), clearly shows that the claimed invention has substantial utility. Applicants submit that the Watson Declaration concludes that the location of a GPCR strongly links that GPCR to its physiological function and states that the relevant art (e.g., Browne, Wilson) supports this conclusion. Applicants submit that the Watson Declaration provides several examples of specific orphan GPCRs correlated with a condition based upon their location in a mammal, including 19AJ/RUP3; 18F; 19Y; 18A; 18AI; 19BX.

Applicants' arguments have been fully considered but are not found persuasive. The 11/2/2000 Watson Declaration was fully considered prior to making the rejection and has been fully considered in response to Applicants' arguments but is not found to be persuasive. The examples provided by Watson are not directly relevant to the utility rejection. The utility rejection is based on the limitation in the claims that reads, "wherein a location of the expression of said endogenous GPCR in a mammalian tissue source is known and said endogenous GPCR has been correlated with at least one mammalian physiological function". The phrase "correlated with at least one mammalian physiological function" broadly encompasses any GPCR wherein only the mammalian tissue source is known.

Applicants state (on page 12) in the response of 3/19/03 that the phrase "correlated with at least one mammalian physiological function" refers to "a receptor that has, for example, been shown to expressed in a location that indicates its function." A "function" indicated by location of expression alone does not lend an orphan GPCR a substantial utility. For example, a GPCR expressed only in the brain could be said to be correlated with brain "function", yet have no substantially utility. In each of the examples provided by Watson, further experimentation has been performed to reasonably correlate the orphan GPCR with a substantial utility. With respect to 19AJ, expression in islets cells did not necessarily indicate that the GPCR functioned in insulin. In order to provide a reasonable correlation between the receptor function and insulin production it was necessary to demonstrate that insulin production was increased when the 19AJ GPCR was introduced into insulin producing cells. With respect to 18F, further experimentation was done to correlate reduction of expression with rapid loss of body weight. With respect to 19Y, 18A, and 18AI, the asserted utility is based on differential expression in tumors, which is different than determining function solely based on expression in normal tissues. 19BX may have a substantial utility as a marker of post-ischemic events; however this is based on correlation with a specific disease condition and not based solely on its expression in normal brain tissue.

A substantial utility is a practical use which amounts to more than a starting point for further research and investigation, and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, a method of screening for inverse agonists of a GPCR wherein constitutive activity of the GPCR is correlated with the onset of a particular disease condition would be a practical use of the material. However, a method of screening a GPCR wherein expression is correlated with "function in the brain" but has no particular correlation with a disease would not constitute a substantial utility. A stated belief that a connection exists between a GPCR and a disease, based solely on location of GPCR expression, is not sufficient information to use the claimed method to identify compounds to treat the disease; it merely

defines a starting point for further research and investigation to determine if there is actually a nexus between the GPCR and the disease. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, also does not constitute a substantial utility. In summary, the instant application has failed to provide information as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility, or a well-established utility. It is maintained that the proposed use of the claimed invention is simply a starting point for further research and investigation into potential practical uses of the claimed method.

Claim Rejections - 35 USC § 112, 1st paragraph

Claims 34, 40 and 45-70 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Applicants' arguments (10/18/05; pg 11) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 10/18/05, Applicants submit that the claimed invention has utility as described at pgs 7-11.

Applicants' arguments have been fully considered but are not found persuasive. The claimed invention lacks utility for the reasons set forth in the previous office action and reiterated above. Therefore, one skilled in the art would not know how to use the claimed invention.

Even if a specific and substantial asserted utility or a well established utility were to be established, the claims would remain rejected under 35 U.S.C. 112, 1st paragraph because the specification while enabling for -

1) a method of screening with a constitutively activated GPCR, wherein the GPCR has been constitutively activated by altering the third position removed from

the beginning of the transmembrane domain represented by alignment with position 293 in the α1β-adrenergic receptor;

2) a method of screening with a constitutively activated orphan GPCR, wherein the orphan GPCR contains the sequence DRY in the second intracellular loop and is activated by mutating D to any other amino acid;

3) a method of screening with a constitutively activated orphan GPCR, wherein the orphan GPCR is constitutively activated by overexpression;

4) a method of screening with an endogenous constitutively active orphan GPCR or endogenous orphan GPCR subjected to constitutive activation, wherein the orphan GPCR has been "correlated with a physiological function" by correlation with tissue expression.

does not reasonably provide enablement for -

1) a method of screening with a constitutively activated orphan GPCR, wherein the orphan GPCR is constitutively activated by any other mechanism;

2) a method of screening with an endogenous constitutively active orphan GPCR or endogenous orphan GPCR subjected to constitutive activation, wherein the orphan GPCR has been "correlated with a physiological function" by any other correlation method.

Applicants' arguments (10/18/05; pg 12-16) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

With respect to constitutive activation of orphan GPCRs, Applicants argue in the response dated 10/18/05 that the claims are fully enabled. Applicants argue that one of ordinary skill in the art would be able to, without undue experimentation, constitutively activate an orphan GPCR by any mechanism taught in the specification or known in the art at the time. Applicants argue that is not required that they list every possible method for constitutively activating a GPCR in order to employ a step comprising such in a patent claim. Applicants argue that the exemplary methods provided for constitutive activation, coupled with those known in the art, meet the burden for enabling the invention. Applicants argue that there is no

structural difference between "orphan" GPCRs and "known" GPCRs, and therefore methods that work for activating "known" GPCRs will work with "orphan" GPCRs. Applicants submit that there is no evidence that these method will not work with "orphan" GPCRs.

Applicants' arguments have been fully considered but are not found persuasive. Applicants appear to be treating all "known" and "orphan" GPCRs as structurally identical molecules that can be constitutively activated by identical mechanisms. However, GPCRs are structurally diverse. For example, Wilson et al 1998 (British Journal of Pharmacology. 125: 1387-1392), teaches, "The superfamily of GPCRs is one of the largest families of genes yet identified" and "These 'orphan' receptors show low levels of homology with known GPCRs (typically less than 40%) too low to classify them with any confidence into a specific receptor subfamily. Many orphan receptors in fact show closer homology to each other than to known GPCRs, suggesting that they may represent new sub-families of receptors with distinct, possibly novel, ligands. These subfamilies are distributed throughout the GPCR superfamily tree, suggesting that they will have a diverse range of functions" (see pg 1387).

Applicants discuss mechanisms of activation of particular GPCRs with known ligands and state that these mechanisms will work with other, structurally different receptors. As stated in the previous action and reiterated herein, there is no evidence that these mechanisms will work predictably with structurally divergent orphan GPCRs. Pages 38-53 of the specification discuss various means of constitutively activating different GPCRs with known ligands. All of these GPCRs and mechanisms are known in the prior art (see specification for references). These include the following mechanisms: mutational cassette (non-transmembrane or transmembrane), truncation of C-terminal tail, point mutations, anti-peptide antibodies, and overexpression. The majority of these mechanisms are specific to a particular species of GPCR. It is not predictable that these mechanisms will work with novel orphan receptors. For example, the specification details 8 non-transmembrane and 4 transmembrane mutational cassettes. Each cassette has

been shown to work with a particular receptor. For example, the specification points to the FCSREKAA cassette, shown to constitutively activate β-adrenergic receptors. As evidence, the specification cites a review by Lefkowitz et al, 1993, that shows that mutations comparable to this cassette activate β2 and α2a-adrenergic receptors. The specification provides no evidence that this cassette will work to constitutively activate any other GPCRs other than adrenergic receptors. For each of the other eleven proposed cassettes, mutations corresponding to the cassette have been shown to constitutively activate a single GPCR. There is no evidence that any of these cassettes will activate any GPCR other than the one they have been shown to work with. In order to use this cassette to predictably activate orphan receptors, one of skill the art would first need to isolate to test a wide range of GPCRs to see whether or not use of this cassette results in constitutive activation of the receptors.

The examiner has noted three mechanisms of constitutive activation of a GPCR that appear to predictably produce a constitutively activated GPCR (the following references were cited in the previous Office Action):

1) Teitler et al (US Patent 6,255,089) teaches that constitutive activation of most GPCRs by mutation of the "third position removed from the beginning of the transmembrane domain" to any other amino acid, with changes to R, K, and E producing the greatest level of activation. This position corresponds to position 293 in the α1β-adrenergic receptor. Similarly, on page 45 of the instant specification, Applicant has provided 9 examples, all found in the prior art, of 9 receptors wherein mutation of an amino acid corresponding to position 293 of the α1β-adrenergic receptor resulted in constitutive activation of the receptor.

2) Scheer et al (February 1997. Proc Natl Acad Sci USA, 94: 808-813) teaches that the position E/DRY is highly conserved in GPCRs and mutation at the D position in the α1β or rhodopsin receptors results in constitutive receptor activation.

3) Pauwels (1998, Mol Neurobiol, 17(1-3): 109-135) reviews on pages 110-114 a large variety of GPCRs that have been constitutively activated by expression in recombinant systems with high levels of expression (overexpression).

None of Applicants' claims are limited to constitutive activation by any of these mechanisms. For example, the only limitation in claim 48 is that the receptor contain the sequence X1BBHyX2 in the 3rd intracellular loop, wherein Hy is alanine (A). Therefore, this claim encompasses receptors with the sequence X1BBAX2 in the 3rd intracellular loop that are constitutively activated by each the three mechanisms described above, but also by any other possible mechanism. However, Applicant has not provided guidance as to what other mechanisms will predictably work to constitutively activate orphan GPCRs with X1BBAX2 in the 3rd intracellular loops. In order to use the full scope of the claimed invention, one of one of ordinary skill it the art would first need to test the other methods of constitutive activation in a number of receptors and determine whether or not the method predictably produces constitutive activity in a representative number of receptors. Without this information, one of ordinary skill in the art would not reasonably believe that the other methods would work to constitutively activate any orphan receptor.

It is acknowledged that the level of skill of those in the art is high, but it is not disclosed and not predictable from the limited teachings of the prior art and specification that the method of the present invention could be used with orphan GPCRs that are constitutively activated by any other method. There are no examples of using this method to screen orphan GPCRs that are constitutively activated by any other method. Thus the specification fails to teach the skilled artisan how to use the method as a screening agent without resorting to undue experimentation. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use the method for the above stated purpose. Due to the large quantity of experimentation necessary to determine if the other mechanisms of constitutive activation could be used in the method for screening, the lack of direction/guidance presented in the specification regarding same, lack of working examples and the teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention. What Applicant has provided is a mere wish or plan and an invitation to experiment.

With respect to correlation with physiological function, Applicants argue that the claimed feature of correlating an orphan GPCR one of ordinary skill in the art would be able to employ various means of correlating an orphan GPCR with physiological function, for example by observing physiological changes in a mammal following suppression of expression of an orphan GPCR. Applicants state that one of ordinary skill in the art could suppress expression of an orphan GPCR in a mammal by use of an antisense oligonucleotide or by gene targeted animals ("knock-outs"). Applicants state that the use of antisense oligonucleotides was well known in the art at the time the invention was made, and gene targeted animals are described in the specification. Applicants also note that the specification shows evidence for a physiological role for GPR3 in epilepsy (It is noted that Applicants refer to the description of GPR3 evidence as being on pg 60, lines 15-23 and Figure 15; however, the Examiner can find no mention of GPR3 at pg 60. It appears that the evidence shown in Figure 15 is described on pg 77, lines 4-6).

Applicants' arguments have been fully considered but are not found persuasive. As set forth in the previous Office Action, all of the claims encompass a method of screening with an orphan GPCR (either endogenous constitutively active, or subjected to constitutive activation), wherein the orphan GPCR has been correlated with a physiological function. The phrase "correlated with physiological function" is broad and ambiguous and encompasses orphan GPCRs that have been correlated with physiological function by correlation with tissue expression, as well as by demonstration of an actual role in a physiological function.

The various means of determining orphan GPCR function referred to by Applicants each constitute undue experimentation. The relevant art teaches the difficulty and unpredictability of using these techniques to determine the function of an unknown gene (e.g., an orphan GPCR). With respect to antisense oligonucleotides (AOs), Van Oekelen et al (2003) teaches "There is sufficient evidence that AOs can be effective in modulating GPCR function. However one has to realize that the antisense technology has a lot of pitfalls and drawbacks (Table

4)...It is becoming clear that incomplete knowledge of the internalization and the mechanisms of action of AOs and the remaining questions concerning specificity and effectiveness have to be overcome before AOs can be used confidently as valuable research (let alone therapeutic) agents" (see pg 136 of Van Oekelen et al, 2003. Brain Research Reviews. 42: 123-142). With respect to "knock-out" animals, Leiter et al 2002, teaches the following: "There are numerous instances to show the ability of the genome to compensate for the loss of certain genes by upregulating related genes in genetically engineered mouse mutants" (see pg 302 of Leiter et al, Diabetologia, 45: 296-308). In view of this, it is unpredictable whether or not a knock-out or reduction in gene expression will have a detectable phenotype.

With respect to association of function by differential tissue expression, Applicants provide data that GPR3 is overexpressed in temporal cortex tissue from epileptic patients, as compared with normal patients (Figure 15). However, one of skill in the art would not conclude that a physiological function had been determined for GPR3 because Applicants have provided a single analysis without any relative range for utility based on overexpression in epileptic tissue. It is unclear whether or not the control sample is matched temporal cortex tissues or represents a pooled brain tissue sample. The specification does not teach what the level of reproducibility or reliability is, whether the results are statistically significant, or the nature or number of samples that were used. It is not clear, for example, if the overexpression was detected in 1 out of 10 or 10 out of 10 epileptic patients. This information is too sparse to allow the polynucleotide to be used as a diagnostic marker for epilepsy. Finally, even if sufficient information was provided that links GPR3 with epilepsy, this single example does not show the predictability of determining any other orphan GPCR function based on tissue expression. The increased expression of GPR3 in epileptic brain tissues appears to be the results of a 'fishing' expedition. GPR3 was expressed in a number of tissues, including the brain, pancreases, thyroid, heart, spleen, lung and liver (Figure 14). GPR6 and GPR12 were also expressed in multiple tissues, including the brain (Figure 14). However, the physiological function of GPR6 or GPR12 remains unpredictable. One could test to see whether or not

they are overexpressed in epileptic tissue as well; but the results are unknowable until this is done. One could examine a wide range of diseased tissues without finding differential expression of these orphan GPCRs. Uhlenbrook et al (Cellular Signaling. 14: 941-953. 2002; cited in the previous Office Action) teaches ligands to GPR3, GPR6, GPR16, but is unable to determine the physiological role of these GPCRs; as Uhlenbrook teaches, "Basal expression of the respective receptors in HUVECs was low and no change (upregulation) could be observed, thus leaving the question for their physiological function unanswered. Gene knockouts and transgenic animals will be required to understand their physiological role" (pg 951). Therefore, even after a large quantity of experimentation, the physiological function of these GPCRs remains unknown and unpredictable, and a further large quantity of experimentation will be required to attempt to determine the physiological role of these GPCRs.

Therefore, it is maintained that in order to practice the claimed invention, one of ordinary skill in the art would first need to correlate an orphan GPCR with a mammalian physiological function by means other than correlation with tissue expression (tissue expression alone would not provide utility, as described above). It is acknowledged that the level of skill of those in the art is high, but it is not disclosed and not predictable from the limited teachings of the prior art and specification how to correlate an orphan GPCR with a physiological function, other than by tissue expression, without undue experimentation. Thus the specification fails to teach the skilled artisan how to use the claimed method over the full scope of the claims without resorting to undue experimentation.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 34, 40 and 45-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments (10/18/05; pg 16-18) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

With respect to constitutive activation of orphan GPCRs, Applicants submit in the 10/18/05 response that the claims are fully described. Applicants submit that one of ordinary skill in the art would have understood that Applicants were in possession of methods for identifying a compound that stimulates an endogenous orphan GPCR, or reduces activity of an active receptor state of an endogenous GPCR, by constitutively activating the orphan GPCR through means other than by the three means acknowledged by the Office Action. Applicants submit that various means of constitutively activating a GPCR are disclosed in the specification. Applicants submit that "orphan" GPCRs and "known" GPCRs (those with a "known" ligand) share all the same "molecular and biochemical features".

Applicants' arguments have been fully considered but are not found persuasive. Applicants' arguments parallel those in the response to the rejection for lack of enablement. GPCRs are a structurally diverse genus of molecules and do not all share the same molecular and biochemical features. The teachings of Wilson cited above indicate the sequence and functional diversity found within the GPCR superfamily. The claims encompass methods comprising constitutively activating an orphan GPCR by any mechanism selected from a number of different mechanisms that have been shown to constitutively activate particular GPCR species. These methods are highly variant because a significant number of different approaches have been used to constitutively activate different receptors. Applicant has provided a variety of teachings for constitutive activation of individual species of GPCRs with known ligands. Applicant has not described constitutive activation of any orphan GPCRs. As noted above in the enablement rejection, three of Applicants teachings with regard to constitutive activation of GPCRs appear to be broadly applicable to orphan receptors. However, Applicants claims are not limited to the genus of

methods encompassing only activation by these methods. Applicants' claims are instead drawn to a much larger genus that includes activation by any possible method, many of which have only been shown to work with a particular species of receptor with a known ligand, and there is no evidence that these mechanisms will work with any orphan GPCR. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Therefore, it is maintained that Applicants were not in possession of the claimed genus.

With respect to orphan GPCRs that are correlated with a physiological function other than by tissue expression, Applicants submit in the 10/18/05 response that a person of ordinary skill in the art would have understood Applicants to possess means of correlating an orphan GPCR with a physiological function. Applicants submit that "various means other than tissue expression are known for correlating an orphan GPCR with a physiological function" including suppression of orphan GPCR expression in mammals.

Applicants' arguments have been fully considered but are not found persuasive. Applicants' arguments parallel those in the response to the rejection for lack of enablement. The genus of orphan GPCRs is large and diverse. Applicants have not provided a description of any orphan GPCRs within this genus that have been correlated with a physiological function. The suppression techniques taught by Applicants do not provide sufficient guidance to determine the physiological function of GPCRs. Instead they only provide in guidance towards possible experimentation that could be performed with orphan GPCRs. Without possession of a GPCR correlated with a physiological function the method could not be practiced as claimed. It is maintained that one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

Claims 40, 53, 55, 56, 58, 60, 68 and 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Gershengorn et al (U.S. Patent 6,087,115), published July 11, 2000 and filed January 22, 1997.

Applicants' arguments (10/18/05; 19-21) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response dated 10/18/05, Applicants argue that Gershengorn does not teach the following limitation of each of the pending claims: "wherein an endogenous ligand for said receptor has not been identified." Applicants submit that Gershengorn does not teach any orphan receptors and does not teach that orphan receptors can be screened by utilizing constitutive activation.

Applicants' arguments have been fully considered but are not found persuasive. It is true that Gershengorn does not use the term "orphan receptor". However, in the Detailed Description of the Invention, Gershengorn teaches the KSHV receptor as an example of a constitutively active receptor that can be used to identify negative antagonists of the receptor. The method taught by Gershengorn does not require that a ligand be identified for the receptor. At the time of filing of the Gershengorn patent application, the ligand for KSHV was not known. It is true that Gershengorn identify molecules that can bind KSHV in Example 1. However, in both the Detailed Description of the Invention, and in Example 2, Gershengorn describes using a receptor (such as KSHV) in a method of screening for antagonists that negatively regulate receptor activation, and the method does not require that the ligand first be identified. Therefore, it is maintained that Gershengorn anticipates the claimed methods.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER